

AMENDMENTS TO THE CLAIMS

The following list of claims replaces all previous sets of claims:

1. (Currently Amended) A virus-like particle (VLP) comprising i) a fusion polypeptide comprising a polypeptide of interest (POI) and a particle-associating portion of ~~[[a]] an~~ avian ~~hepadnavirus~~ large envelope polypeptide (L) or a functional derivative ~~or homolog~~ thereof and ii) ~~[[a]] an~~ avian ~~hepadnavirus~~ small envelope (S) polypeptide or a functional derivative ~~or homolog~~ thereof.
2. (Currently Amended) The VLP of claim 1 comprising a fusion polypeptide comprising a polypeptide of interest (POI) and a particle-associating portion of a large envelope polypeptide (L) of ~~an avian hepadnavirus, such as duck hepatitis B virus (DHBV),~~ or a functional derivative thereof.
3. (Currently Amended) The VLP of claim 1 or 2 comprising a fusion polypeptide comprising a polypeptide of interest (POI) and a particle-associating portion of a large envelope polypeptide (L) of ~~an avian hepadnavirus, such as duck hepatitis B virus (DHBV),~~ or a functional derivative thereof and ii) a small envelope (S) polypeptide of ~~an avian hepadnavirus, such as DHBV,~~ or a functional derivative thereof.
4. (Original) The VLP of claim 1 or 2 wherein the particle-associating portion of L comprises at least the S domain of L, or the S domain of L minus the TM1 domain, or a functional derivative thereof.
5. (Original) The VLP of claim 1 or 2 wherein the POI is located in the pre-S domain of L or at the amino terminal side of the S domain of L, or the S domain minus the TM1 domain of L.
6. (Original) The VLP of claim 1 or 2 wherein the L polypeptide comprises an amino acid sequence substantially as set forth in SEQ ID NO: 7 or SEQ ID NO: 9 or a functional derivative thereof or comprises an amino acid sequence having at least 50% similarity to SEQ ID NO: 7 or SEQ ID NO: 9.

7. (Currently Amended) The VLP of claim 1 ~~[[or 2]]~~ wherein the particle-associating portion of L polypeptide comprises an amino acid sequence ~~substantially as set forth in SEQ ID NO: 7 or SEQ ID NO: 9~~ or a functional derivative thereof comprising an amino acid sequence having at least 50% identity similarity to SEQ ID NO: 7 or SEQ ID NO: 9.
8. (Currently Amended) The VLP of claim 1 or 2 wherein the particle-associating portion of L polypeptide comprises or consists essentially of amino acids 24 to 107 of SEQ ID NO: 9 or an amino acid sequence having at least 50% identity similarity thereto.
9. (Currently Amended) The VLP of claim 1 ~~any one of claims 1 to 9~~ wherein the L polypeptide is a DHBV L polypeptide or functional derivative thereof.
10. (Currently Amended) The VLP of claim 1 ~~[[or 2]]~~ wherein said L polypeptide or particle-associating portion thereof is encoded by a sequence of nucleotides ~~substantially as set forth in SEQ ID NO: 6 or SEQ ID NO: 8~~ or having at least about 50% identity similarity to SEQ ID NO: 6 or SEQ ID NO: 8 or a contiguous sequence of nucleotides capable of hybridizing to a complementary form of SEQ ID NO: 6 or SEQ ID NO: 8 under hybridisation conditions of medium stringency.
11. (Original) The VLP of claim 1 or 2 wherein the L polypeptide further comprises a signal sequence.
12. (Currently Amended) An isolated or recombinant polypeptide for use in the assembly of a VLP, comprising a polypeptide of interest (POI) and at least a particle-associating portion of a large envelope polypeptide (L) of an avian hepadnavirus, ~~such as DHBV,~~ or a functional derivative thereof, wherein the POI is not a pre-S region of an avian hepadnavirus.
13. (Currently Amended) A recombinant polypeptide capable of assembling into a VLP when expressed in a cell comprising a polypeptide of interest (POI) and at least a particle-associating portion of a large envelope polypeptide (L) of an avian hepadnavirus ~~such as DHBV~~ or a functional derivative thereof, wherein the POI is not a pre-S region of an avian

hepadnavirus.

14. (Original) The polypeptide of claim 12 or 13 wherein the particle-associating portion of L comprises at least the S domain of L, or the S domain of L minus the TM1 domain, or a functional derivative thereof,
15. (Original) The polypeptide of claim 12 or 13 wherein the POI is located in the pre-S domain of L or at the amino terminal side of the S domain of L, or the S domain minus the TM1 domain of L.
16. (Currently Amended) The ~~recombinant or isolated~~ polypeptide of claim 12 or 13 wherein the L polypeptide comprises an amino acid sequence ~~substantially as set forth in SEQ ID NO: 7 or SEQ ID NO: 9 or a functional derivative thereof or comprises an amino acid sequence having at least 50% identity similarity to SEQ ID NO: 7 or SEQ ID NO: 9.~~
17. (Currently Amended) The ~~recombinant or isolated~~ polypeptide of claim 12 or 13 wherein the particle-associating portion of L polypeptide consists of an amino acid sequence ~~substantially as set forth in SEQ ID NO: 7 or SEQ ID NO: 9 or a functional derivative thereof comprising an amino acid sequence having at least 50% identity similarity to SEQ ID NO: 7 or SEQ ID NO: 9.~~
18. (Currently Amended) The ~~recombinant or isolated~~ polypeptide of claim 12 or 13 wherein the particle-associating portion of L-polypeptide comprises or consists essentially of amino acids 24 to 107 of SEQ ID NO: 9 or an amino acid sequence having at least 50% ~~similarity~~ identity thereto.
19. (Currently Amended) The recombinant or isolated polypeptide of claim 12 or 13 wherein said L polypeptide or particle-associating portion thereof is encoded by a sequence of nucleotides ~~substantially as set forth in SEQ ID NO: 6 or SEQ ID NO: 8 or having at least about 50% identity similarity to SEQ ID NO: 6 or SEQ ID NO: 8 or a contiguous sequence of nucleotides capable of hybridizing to a complementary form of SEQ ID NO: 6 or SEQ ID~~

NO: 8 under hybridisation conditions of medium stringency.

20. (Currently Amended) The ~~recombinant or isolated~~ polypeptide according to claim 12 or 13 wherein said L polypeptide further comprises a signal sequence.
21. (Currently Amended) The ~~recombinant or isolated~~ polypeptide of claim 12 or 13 wherein the L polypeptide is a DHBV L polypeptide or a functional derivative thereof.
22. (Currently Amended) A recombinant nucleic acid molecule for use in making a VLP, said nucleic acid molecule comprising a contiguous sequence of nucleotides encoding a fusion protein comprising a polypeptide of interest (POI) and at least a particle-associating portion of an L polypeptide of an avian hepadnavirus, ~~such as DHBV~~, or a functional derivative thereof, wherein the POI is not a pre-S region of an avian hepadnavirus.
23. (Currently Amended) A recombinant nucleic acid molecule for use in making a VLP, said nucleic acid molecule comprising a contiguous sequence of nucleotides encoding i) a fusion polypeptide comprising a polypeptide of interest (POI) and at least a particle-associating portion of an L polypeptide of an avian hepadnavirus, ~~such as DHBV~~, or a functional derivative thereof, and ii) a small envelope (S) polypeptide of an avian hepadnavirus ~~such as DHBV~~ or a functional derivative thereof, wherein the POI is not a pre-S region of an avian hepadnavirus.
24. (Original) The nucleic acid molecule of claim 22 or 23 wherein the particle-associating portion of L comprises at least the S domain of L, or the S domain of L minus the TM1 domain, or a functional derivative thereof.
25. (Original) The nucleic acid molecule of claim 22 or 23 wherein the POI is located in the pre-S domain of L or at the amino terminal side of the S domain of L, or the S domain minus the TM1 domain of L.
26. (Currently Amended) The nucleic acid molecule of claim 22 or 23 which encodes an L

polypeptide comprising an amino acid sequence substantially as set forth in SEQ ID NO: 7 or SEQ ID NO: 9 or comprises an amino acid sequence having at least 50% identity ~~similarity~~ to SEQ ID NO: 7 or SEQ ID NO: 9.

27. (Currently Amended) The nucleic acid molecule of claim 26 which encodes a particle associating portion of L polypeptide consisting essentially of amino acids 24 to 167 of SEQ ID NO: 9 or an amino acid sequence having at least 50% identity ~~similarity~~ to SEQ ID NO: 9.
28. (Currently Amended) The nucleic acid molecule of claim 22 or 23 wherein said L polypeptide or particle associating portion thereof is encoded by a sequence of nucleotides ~~substantially as set forth in SEQ ID NO: 6 or SEQ ID NO: 8 or having at least about 50%~~ identity ~~similarity~~ to SEQ ID NO: 6 or SEQ ID NO: 8 or a contiguous sequence of nucleotides capable of hybridizing to a complementary form of SEQ ID NO: 6 or SEQ ID NO: 8 under hybridisation conditions of medium stringency.
29. (Original) The nucleic acid molecule of claim 22 or 23 wherein the L polypeptide further comprises a signal sequence.
30. (Original) The nucleic acid molecule of claim 22 or 23 wherein the L polypeptide is a DHBV L polypeptide or functional derivative thereof.
31. - 39. (Cancelled).
40. (Original) An isolated and/or recombinant cell comprising the nucleic acid molecule of any one of claims 22 to 30 or expressing the polypeptide of any one of claims 12 to 21 or the VLP of any one of claims 1 to 11.
41. (Original) The cell according to claim 40 wherein said cell is a eukaryotic cell, preferably a yeast, avian or mammalian cell.

42. (Currently Amended) A method of delivering a POI to a subject or cell comprising expressing the POI in a VLP comprising L polypeptide from an avian hepadnavirus, ~~such as DHBV,~~ or a functional derivative thereof such that at least part of the POI is expressed on the surface of the VLP and administering the VLP to a subject or cell.
43. (Original) The method of claim 42 wherein the VLP is made in an *in vitro* expression system such as a yeast, avian or mammalian expression system.
44. (Original) The method of claim 42 wherein the VLP is made *in vivo* in the cells of a subject after administration of the nucleic acid molecule of any one of claims 22 to 30.
45. (Original) A method for making a recombinant VLP said method comprising:
cloning a nucleic acid molecule encoding a polypeptide of interest into an
- i) expression vector comprising a particle-associating portion of an L polypeptide of an avian hepadnavirus, such as DHBV, or a functional derivative thereof;
 - ii) introducing the recombinant expression vector of step i) into a suitable cell and maintaining same under conditions which allow protein expression and particle assembly with S polypeptide of an avian hepadnavirus, such as DHBV, or a functional derivative thereof; and
 - iii) recovering said virus-like particles from said cells.